

## PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

REC'D 24 FEB 2005

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(PCT Article 36 and Rule 70)

01 APR 2005

Applicant's or agent's file reference 2031250PC/or	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/FI2003/000726	International filing date (day/month/year) 03.10.2003	Priority date (day/month/year) 03.10.2002
International Patent Classification (IPC) or national classification and IPC C07K 7/06, A61K 38/08, A61P 35/00		
Applicant KARYON OY et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
  - a. ☒ (sent to the applicant and to the International Bureau) a total of 3 sheets, as follows:
    - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s))  
\_\_\_\_\_, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

## 4. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

Date of submission of the demand 29.03.2004	Date of completion of this report 02.02.2005
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# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI2003/000726

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ the international application as originally filed/furnished

- ☒ the description:

pages 1-92 \_\_\_\_\_ as originally filed/furnished

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☒ the claims:

pages \_\_\_\_\_ as originally filed/furnished

pages\* \_\_\_\_\_ as amended (together with any statement) under Article 19

pages\* 93-95 received by this Authority on 03.02.2005

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☐ the drawings:

pages \_\_\_\_\_ as originally filed/furnished

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages \_\_\_\_\_

☐ the claims, Nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (specify): \_\_\_\_\_

☐ any table(s) related to the sequence listing (specify): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages \_\_\_\_\_

☐ the claims, Nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (specify): \_\_\_\_\_

☐ any table(s) related to the sequence listing (specify): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 25-27

because:

☒ the said international application, or the said claims Nos. 25-27  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the  
Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with  
the technical requirements provided for in the Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI2003/000726

**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	<u>1-24</u>	YES
	Claims	_____	NO
Inventive step (IS)	Claims	<u>1-24</u>	YES
	Claims	_____	NO
Industrial applicability (IA)	Claims	<u>1-24</u>	YES
	Claims	_____	NO

## 2. Citations and explanations (Rule 70.7)

The claims relate to tumour targeting units and their use.

The following documents were found:

A US 5981478

B US 5622699

C EP 271041

D US 6083913

Document A describes integrin binding peptides.

Document B relates to a method of identifying a molecule that homes specifically to one or a few selected organs. The molecules can be used to direct a moiety to the selected organ. They can be linked to labels and pharmaceuticals to use in the treatment of cancer (see columns 12-13). However, the organ specific peptides have not been shown to be tumour targeting. Peptide no. 3, that resembles the claimed peptides is described as a brain homing.

Document C discloses atrial peptide derivatives.

Document D discloses peptides that bind to the thrombopoietin receptor.

The documents show the general state of the art.

Thus, claims 1-24 are considered to fulfil the requirements of novelty, inventive step and industrial applicability.

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# CLAIMS

1. A tumor targeting unit comprising a peptide sequence:



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or a pharmaceutically or physiologically acceptable salt thereof, wherein,

Dd-Ee-Ff is Aa-Bb-Cc, Cc-Bb-Aa, Bb-Cc-Aa, Aa-Cc-Bb, Cc-Aa-Bb or Bb-Aa-Cc, wherein

10 Aa, is isoleucine, leucine or *tert*-leucine, or a structural or functional analogue thereof;

Bb is arginine, homoarginine or canavanine, or a structural or functional analogue thereof;

15 Cc is glutamic acid or aspartic acid, or a structural or functional analogue thereof;

Rr are each, independently, any amino acid residue or structural or functional analogues thereof;

n and m are, independently, 0-7, and the sum of n and m does not exceed seven; and,

20 Cy and Cyy are entities capable of forming a cyclic structure through an amide or ester bond, or through a hydrazone-like structure.

2. The tumor targeting unit according to claim 1, wherein Dd-Ee-Ff is Aa-Bb-Cc or Cc-Bb-Aa.

25 3. The tumor targeting unit according to any of claim 1 or 2, wherein the peptide is cyclic or forms part of a cyclic structure.

4. The tumor targeting unit according to claim 3, wherein the cyclic structure is a lactam or a lactone.

30 5. The tumor targeting unit according to any one of claims 1 to 4, wherein wherein one of Cy and Cyy is aspartic acid, glutamic acid or a structural or functional analogue thereof, and the other is lysine, ornithine or a structural or functional analogue thereof.

6. The tumor targeting unit according to claim 5, wherein the sum of n and m is two.

35 7. The tumor targeting unit according to any one of claims 1 – 5, wherein Rr<sub>n</sub> and Rr<sub>m</sub> are absent.

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8. The tumor targeting unit according to any one of claims 1 – 7, wherein Rr is any amino acid residue, except histidine or lysine.

9. The tumor targeting unit according to claim 8, wherein Rr is  
5 selected from the group consisting of glycine, arginine and structural or functional analogues thereof.

10. The tumor targeting unit according to any one of claims 1 to 9, wherein Dd-Ee-Ff is IRE, LRE, LRD or ERI or a structural or functional analogue thereof.

11. The tumor targeting unit according to claim 5 having the formula  
10 selected from the group consisting of DIREK (SEQ ID NO. 3), DERIK (SEQ ID NO. 4) and being cyclic by virtue of a lactam bond between D and K.

12. The tumor targeting unit according to any one of claims 1 or 2  
15 having the formula selected from the group consisting of IQLRD (SEQ ID NO. 5), IQLRDWGFIL (SEQ ID NO. 6), LRELS (SEQ ID NO. 7) and LRELSMGYFK (SEQ ID NO. 8).

13. The tumor targeting unit according to any of the previous claims, wherein the unit is derivatized, activated, protected, resin bound or other support bound.

14. A tumor targeting agent comprising at least one targeting unit of  
20 any of claims 1 to 13, directly or indirectly coupled to at least one effector unit.

15. The tumor targeting agent according to claim 14, wherein the effector unit is a directly or indirectly detectable agent or a therapeutic agent.

16. The tumor targeting agent according to claim 15, wherein the  
25 detectable agent comprises an affinity label, a fluorescent or luminescent label, a chelator, a metal complex, an enriched isotope, radioactive material or a paramagnetic substance.

17. The tumor targeting agent according to claim 16, wherein the detectable agent is a rare earth metal.

18. The tumor targeting agent according to claim 17, wherein the  
30 detectable agent is gadolinium.

19. The tumor targeting agent according to claim 15, wherein the therapeutic agent is selected from the group consisting of cytotoxic and cytostatic substances and radiation emitting substances.

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20. The tumor targeting agent according to claim 19, wherein the therapeutic agent is selected from the group consisting of doxorubicin, daunorubicin, methotrexate or boron.

21. A diagnostic or pharmaceutical composition comprising at least one targeting unit according to any one of claims 1 to 13, or at least one targeting agent according to any one of claims 14 to 20.

22. Use of a targeting unit according to any one of claims 1 to 13, or a targeting agent according to any one of claim 14 to 20 for the preparation of a medicament for the treatment of cancer or cancer related diseases.

23. The use according to claim 22, wherein said cancer is a solid tumor.

24. The use according to claim 23, wherein the cancer is selected from the group consisting of carcinoma, sarcoma, melanoma or metastases.

25. A method for treating cancer or cancer related diseases, comprising providing to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition according to claim 21.

26. The method according to claim 26, wherein said cancer or cancer related disease is a solid tumor.

27. The method according to claim 26, wherein said solid tumor is selected from the group consisting of carcinoma, sarcoma, melanoma or metastases.